

Inventor: Leonard KATZ and Peter REVILL Title: PRODUCTION OF POLYKETIDES

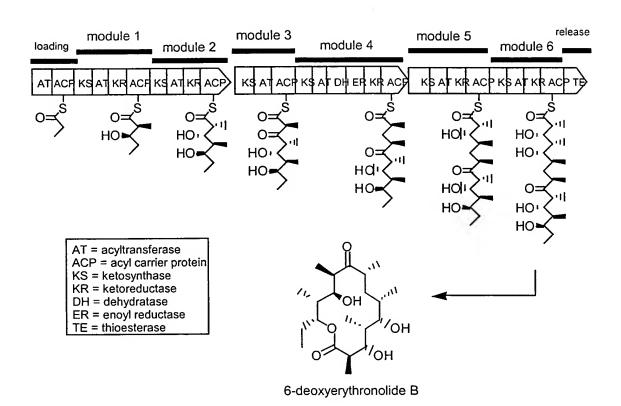


Figure 1



App No.: 10/607,809

Docket No.: 300622004810

Inventor: Leonard KATZ and Peter REVILL Title: PRODUCTION OF POLYKETIDES

Figure 2



App No.: 10/607,809 Docke Inventor: Leonard KATZ and Peter REVILL Title: PRODUCTION OF POLYKETIDES

gaac gaaa tcat	tccti ccgc gtag	ta to cc ag cc ag	ccgg gcgg gatt	acgad agcgd tcggd	c togo c tg	gacci agati aacti tcgg	tggt cctc ggtc ccta	acc cac	ctaa tgat gatc qcqt	gcg cag ccg gct	gaga gtaa atto ccgc gc g V	ggato gtgao ggtga tg go	et t ec a at c	catto tgcg	egatg tgtcc gttag ac	180
gtg Val 5	gaa Glu	ctc Leu	gcg Ala	gac Asp	agg Arg 10	gct Ala	cga Arg	cga Arg	cgc Arg	gcg Ala 15	tgc Cys	cgg Arg	ctg Leu	ctc Leu	agg Arg 20	402
cgt Arg	tgg Trp	ctg Leu	Xb gcc Ala	and a	acg Thr	cac His	act Thr	ccg Pro	gtg Val 30	gag Glu	ccc Pro	ggc Gly	ccg Pro	ctg Leu 35	tcc Ser	450
ctg Leu	cgg Arg	atc Ile	ggc Gly 40	ccg Pro	gtg Val	cgg Arg	gtg Val	tcg Ser 45	gcc Ala	gag Glu	gtc Val	gct Ala	tac Tyr 50	cgc Arg	tcg Ser	498
ccg Pro	acg Thr	ggc Gly 55	gcc Ala	cac His	gly ggg	ttc Phe	ggc Gly 60	ccg Pro	atc Ile	cgc Arg	gtc Val	ctc Leu 65	gat Asp	gcc Ala	gag Glu	546
ggt Gly	gtg Val 70	ccg Pro	gtg Val	gcg Ala	ctc Leu	gcc Ala 75	gat Asp	ccg Pro	gtg Val	ctg Leu	ctg Leu 80	gcg Ala	gcc Ala	gcc Ala	tgc Cys	594
tcg Ser 85	gcg Ala	gac Asp	tcg Ser	cgg Arg	agc Ser 90	cgc Arg	tcg Ser	ctg Leu	ccg Pro	agc Ser 95	gcg Ala	ccg Pro	atc Ile	aac Asn	gcc Ala 100	642
ccg Pro	gac Asp	gcc Ala	ggt Gly	acc Thr 105	gct Ala	gtc Val	gac Asp	tgg Trp	gtg Val 110	ьeu	tcg Ser	tcg Ser	ctc Leu	gcc Ala 115	gac Asp	690
gac Asp	gag Glu	gac Asp	gac Asp 120	Glu	gtg Val	ccc Pro	gcc Ala	ggc Gly 125	Met	acc Thr	gcg Ala	gag Glu	gag Glu 130	gcg Ala	gtg Val	738
cgc Arg	ctg Leu	ctg Leu 135	Ser	cgg Arg	cag Gln	gtc Val	gac Asp 140	gac Asp	ctg Leu	g ccg	g cgg Arg	tcg Ser 145	PIC	g ggc	gcc Ala	786
gac Asp	ccg Pro 150	Trp	tcg Ser	ctg Leu	gtc Val	gco Ala 155	Gly	ccg	g cto Lev	g gcg n Ala	g gcc A Ala 160	, тте	ggg	g cgg / Arg	ttc Phe	834
999 Gly 165	Arg	gcc Ala	ggg Gl <sub>}</sub>	g ato	gco Ala 170	a Asp	gag Glu	tgo Cys	e tgg Tr	ttq Lei 17	ı Let	g gag 1 Glu	gtg Vai	g cto l Lev	gcc Ala 180	882



ggg cg	gg c	tc d	Arg .	gcg Ala 185	gtc Val	gac Asp	gac ( Asp	Asp	ctg Leu 190	tcc Ser	cgc Arg	tcg Ser		ctg Leu 195	agc Ser	930
agt co Ser P	cg a ro T	hr	ctc Leu 200	gcc Ala	gac Asp	cgc Arg	Ala	gtg Val 205	ctc Leu	gtg Val	ggt Gly	gag Glu	999 Gly 210	ttg Leu	cgc Arg	978
tac co	rg E	ccg Pro 215	gat Asp	gtg Val	cgg Arg	ccg Pro	gtg Val 220	ccg Pro	ttc Phe	gac Asp	gtg Val	ccg Pro 225	aac Asn	ccg <sup>.</sup>	ctg Leu	1026
cac g His G 2	ag g lu (	ggc 31y	aag Lys	tcc Ser	gac Asp	gtc Val 235	ccg Pro	ccg Pro	ccg Pro	ccc Pro	gtg Val 240	ccc Pro	gtg Val	ctg Leu	ggc Gly	1074
ggg c Gly P 245	cg '	tgg Trp	tcg Ser	ctg Leu	cgt Arg 250	ccg Pro	gtc Val	gag Glu	gtc Val	gcg Ala 255	gtc Val	cac His	Gly aaa	gat Asp	ggc Gly 260	1122
ggg c	ro .	gac Asp	gtc Val	gca Ala 265	ctg Leu	gtg Val	cac His	cgc Arg	tgg Trp 270	MEC	aac Asn	acc Thr	ccg Pro	cac His 275		1170
gcg ( Ala H	cac His	cac His	tgg Trp 280	Asn	cag Gln	gcg Ala	tgg Trp	ccg Pro 285	neu	gag Glu	cgc Arg	tgg Trp	cgg Arg 290		gaa Glu	1218
ctc q	gcc Ala	cac His 295	cag Gln	ctc Leu	ggc Gly	ggt Gly	gag Glu 300	His	tcc Ser	cto Lev	g ccc l Pro	tgc Cys 305	, vu	gto Val	gga L Gly	1266
cac (	gag Glu 310	gga Gly	cgc	gag Glu	g gto val	gcg L Ala 319	туг	ctg Lev	gag Glu	g cto 1 Le	tao 1 Ty: 320		gtg Val	g ace	c cgc	1314
gac Asp 325	Hind aag Lys			g ggo a Gly	tgo 7 Cy:	s Ty	c ccg	tac Tyi	gg:	g ccg y Pro 33	O MI.	c gad s Asp	c cto Lev	u Gl	g gto y Val	
cac His	atc Ile	gcg	g ato	= gg = Gl; 34	λ GT.	g cg	g gaq g Gli	g gto ı Vai	g ct l Le 35	u GI	g cg y Ar	c gg g Gl	t tt y Ph	c gg e Gl 35	g tc y Se 5	g 1410 r
tcg Ser	ctg Leu	ct <u>c</u> Lei	g cg ı Ar 36	g Al	g gt a Va	c gc l Al	g gg a Gl	t gc y Al 36	а ье	g ct u Le	g ga u As	c gc p Al	c ga a As 37	P	g cg o Ar	g 1458 g
tgc Cys	gcg Ala	cg Arg	g Va	g gt l Va	c gc l Al	c ga a Gl	g cc u Pr 38	O AS	t gt n Va	g ca 1 Hi	ıc aa .s As	ic ga sn Gl 38	u	t to a Se	g gt er Va	g 1506 1



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cgc gcc ttc Arg Ala Phe 390	gcc aag gcc Ala Lys Ala	ggg ttc gtc Gly Phe Val 395	c cgg gag l Arg Glu	agg gag ato Arg Glu Ile 400	ggc ctg Gly Leu	1554
ccc gcc aag Pro Ala Lys 405	aac tcg gct Asn Ser Ala 410	Leu Met Va	c ttc tcc l Phe Ser 415	cgg gtc t g Arg Val (SE	gacgaccggt EQ ID NO:2)	1604
ggttagcctt ctgaccacag tacaacaccg gccctgcggt gacgagccgc	tgtgaacgcg tacttttattg gegagtaggg cgggggggggggggggggggggggggggggg	tggagaacg a atctggttc g gagatcagc g gaggccgag g gagccggag g	tgccggagc cccagcaac gcccggtgg cgctgcgag	geteegeegt tegaceggae ageeggtggt ceegegtggt	gtcgttgccg gaacccgatc gttcgagcag cgtcgacggc	1724 1784 1844 1904



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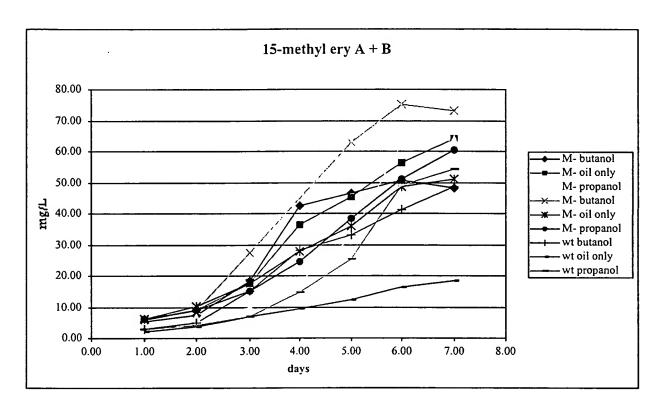
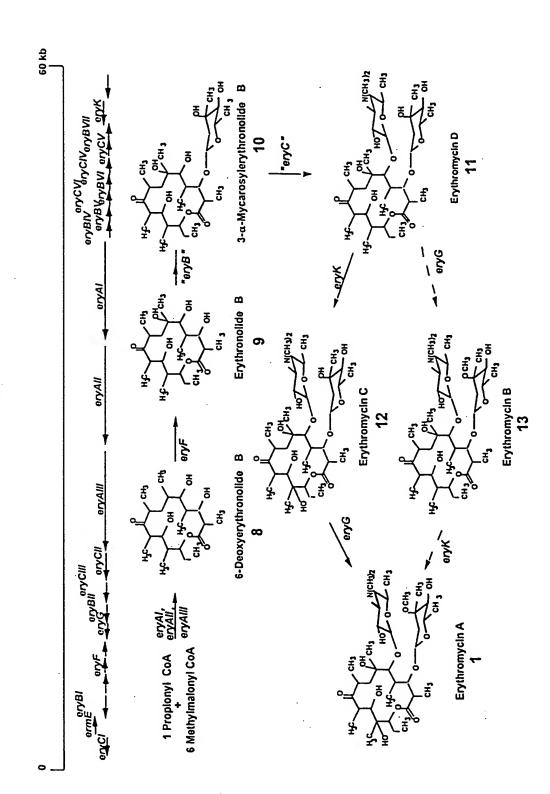


Figure 4



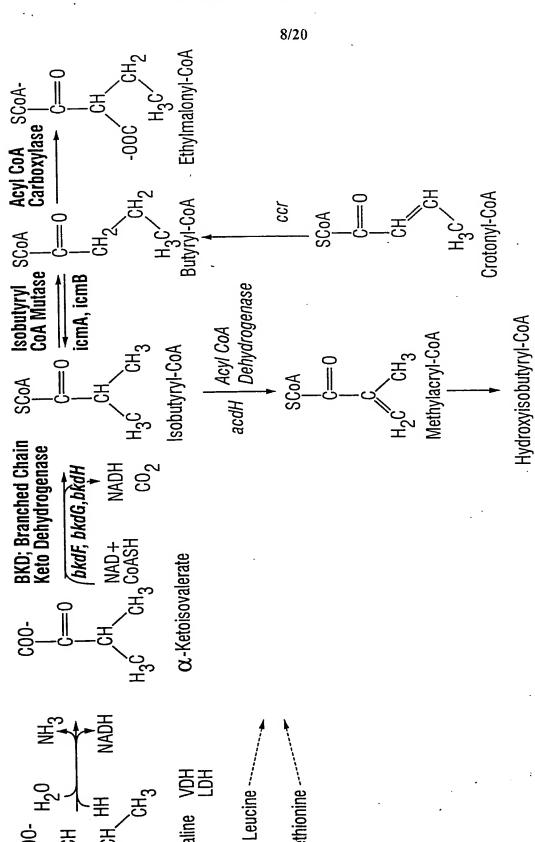


Figure 6 A



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10/20

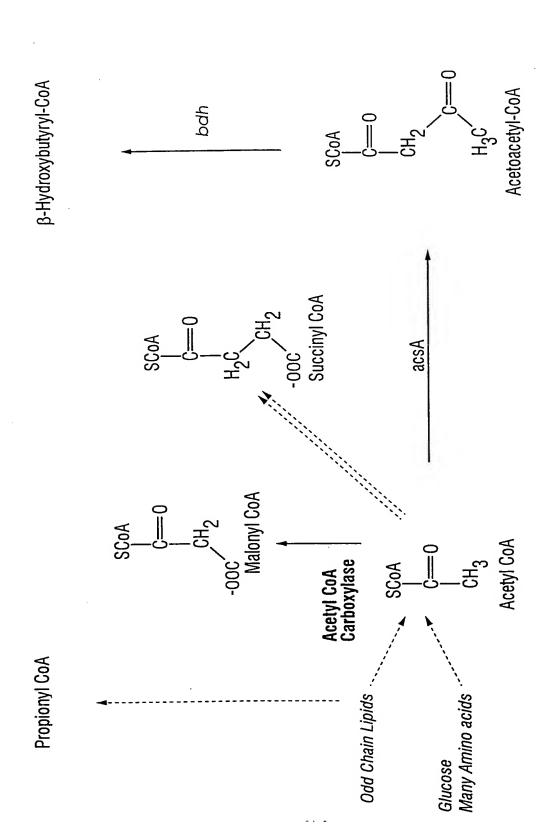


Figure 6 C



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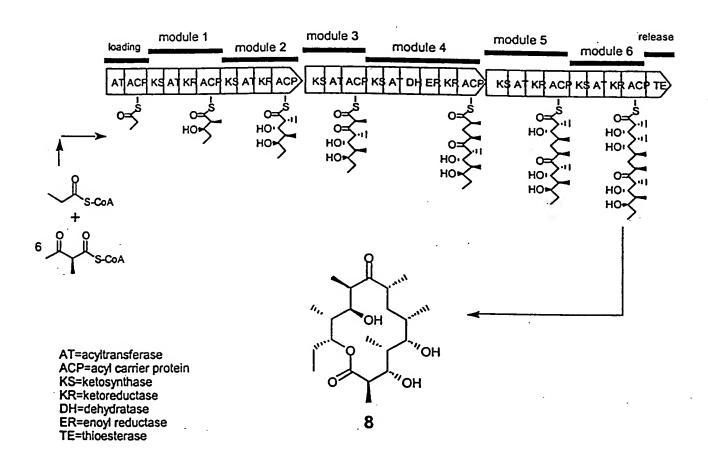


Figure 7



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Figure 8



App No.: 10/607,809 Docke Inventor: Leonard KATZ and Peter REVILL Title: PRODUCTION OF POLYKETIDES

Figure 9



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#### 14/20

Met His Val Pro Gly Glu Glu Asn Gly His Ser Ile Ala Ile Val Gly 10 Ile Ala Cys Arg Leu Pro Gly Ser Ala Thr Pro Gln Glu Phe Trp Arg 25 Leu Leu Ala Asp Ser Ala Asp Ala Leu Asp Glu Pro Pro Ala Gly Arg 40 Phe Pro Thr Gly Ser Leu Ser Ser Pro Pro Ala Pro Arg Gly Gly Phe Leu Asp Ser Ile Asp Thr Phe Asp Ala Asp Phe Phe Asn Ile Ser Pro Arg Glu Ala Gly Val Leu Asp Pro Gln Gln Arg Leu Ala Leu Glu Leu 90 Gly Trp Glu Ala Leu Glu Asp Ala Gly Ile Val Pro Arg His Leu Arg 105 Gly Thr Arg Thr Ser Val Phe Met Gly Ala Met Trp Asp Asp Tyr Ala 120 His Leu Ala His Ala Arg Gly Glu Ala Ala Leu Thr Arg His Ser Leu 140 135 Thr Gly Thr His Arg Gly Met Ile Ala Asn Arg Leu Ser Tyr Ala Leu 155 150 Gly Leu Gln Gly Pro Ser Leu Thr Val Asp Thr Gly Gln Ser Ser Ser 170 Leu Ala Ala Val His Met Ala Cys Glu Ser Leu Ala Arg Gly Glu Ser 185 Asp Leu Ala Leu Val Gly Gly Val Asn Leu Val Leu Asp Pro Ala Gly 200 Thr Thr Gly Val Glu Arg Phe Gly Ala Leu Ser Pro Asp Gly Arg Cys 215 Tyr Thr Phe Asp Ser Arg Ala Asn Gly Tyr Ala Arg Gly Glu Gly Gly 235 230 Val Val Val Leu Lys Pro Thr His Arg Ala Leu Ala Asp Gly Asp 250 245 Thr Val Tyr Cys Glu Ile Leu Gly Ser Ala Leu Asn Asn Asp Gly Ala 265 Thr Glu Gly Leu Thr Val Pro Ser Ala Arg Ala Gln Ala Asp Val Leu 280 Arg Gln Ala Trp Glu Arg Ala Arg Val Ala Pro Thr Asp Val Gln Tyr 300 295 Val Glu Leu His Gly Thr Gly Thr Pro Ala Gly Asp Pro Val Glu Ala 315 310 Glu Gly Leu Gly Thr Ala Leu Gly Thr Ala Arg Pro Ala Glu Ala Pro 330 Leu Leu Val Gly Ser Val Lys Thr Asn Ile Gly His Leu Glu Gly Ala 345 Ala Gly Ile Ala Gly Leu Leu Lys Thr Val Leu Ser Ile Lys Asn Arg 360 His Leu Pro Ala Ser Leu Asn Phe Thr Ser Pro Asn Pro Arg Ile Asp 380 375 Leu Asp Ala Leu Arg Leu Arg Val His Thr Ala Tyr Gly Pro Trp Pro 390 395 Ser Pro Asp Arg Pro Leu Val Ala Gly Val Ser Ser Phe Gly Met Gly 405 410



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#### 15/20

Gly Thr Asn Cys His Val Val Leu Ser Glu Leu Arg Asn Ala Gly Gly 425 420 Asp Gly Ala Gly Lys Gly Pro Tyr Thr Gly Thr Glu Asp Arg Leu Gly 445 440 Ala Thr Glu Ala Glu Lys Arg Pro Asp Pro Ala Thr Gly Asn Gly Pro 460 455 Asp Pro Ala Gln Asp Thr His Arg Tyr Pro Pro Leu Ile Leu Ser Ala 475 470 Arg Ser Asp Ala Ala Leu Arg Ala Gln Ala Glu Arg Leu Arg His His-490 485 Leu Glu His Ser Pro Gly Gln Arg Leu Arg Asp Thr Ala Tyr Ser Leu 505 Ala Thr Arg Arg Gln Val Phe Glu Arg His Ala Val Val Thr Gly His 520 525 Asp Arg Glu Asp Leu Leu Asn Gly Leu Arg Asp Leu Glu Asn Gly Leu 540 535 Pro Ala Pro Gln Val Leu Leu Gly Arg Thr Pro Thr Pro Glu Pro Gly 550 555 Gly Leu Val Phe Val Phe Pro Gly Gln Gly Pro Gln Trp Arg Gly Met 570 565 Gly Val Glu Leu Met Ala Ala Ser Pro Val Phe Ala Ala Arg Met Arg 585 Gln Cys Ala Asp Ala Leu Ile Pro His Thr Gly Trp Asp Pro Ile Ala 600 Met Leu Asp Asp Pro Glu Val Thr Arg Arg Val Asp Val Val His Pro 620 615 Val Cys Trp Ala Val Met Val Ser Leu Ala Ala Val Trp Glu Ala Ala 635 630 Gly Val Arg Pro Asp Ala Val Ile Gly His Ser Gln Gly Glu Ile Ala 650 Ala Ala Cys Val Ala Gly Ala Leu Thr Leu Glu Asp Gly Ala Arg Leu 665 Val Ala Leu Arg Ser Val Leu Leu Leu Arg Glu Leu Ala Gly Arg 680 Gly Ala Met Gly Ser Val Ala Leu Pro Ala Ala Asp Val Glu Ala Asp 700 695 Ala Ala Arg Ile Asp Gly Val Trp Val Ala Gly Arg Asn Gly Ala Thr 715 710 Thr Thr Thr Val Ala Gly Arg Pro Asp Ala Val Glu Thr Leu Ile Ala 730 725 Asp Tyr Glu Ala Arg Gly Val Trp Val Arg Arg Ile Ala Val Asp Cys 745 Pro Thr His Thr Pro Phe Val Asp Pro Leu Tyr Asp Glu Leu Gln Arg 760 Ile Val Ala Asp Thr Thr Ser Arg Thr Pro Glu Ile Pro Trp Phe Ser 775 Thr Ala Asp Glu Arg Trp Ile Asp Ala Pro Leu Asp Asp Glu Tyr Trp 795 790 Phe Arg Asn Met Arg His Pro Val Gly Phe Ala Thr Ala Val Thr Ala 810 805 Ala Arg Glu Pro Gly Asp Thr Val Phe Val Glu Val Ser Ala His Pro 820 825



	eu Pro Ala 35	Ile Asp	Gly 840	Ala	Thr	Val	Ala	Thr 845	Leu	Arg	Arg
Gly Gly G 850	ly Val His	Arg Leu 855	Leu	Thr	Ala	Leu	Ala 860	Glu	Ala	His	Thr
Thr Gly V 865	al Pro Val	Asp Trp 870	Ala	Ala	Val	Val 875	Pro	Ala	Thr	Ala	Thr 880
Ala His A	sp Leu Pro 885	Thr Tyr	Ala	Phe	His 890	His	Glu	Arg	Tyr	Trp 895	Ile
Ser His T	rp Leu Pro	Ser Gly	Glu	Ala 905	His	Pro	Arg	Pro	Ala 910	Asp	Asp
	Ser Gly Thr 915	Gly Arg	Thr 920	Glu	Ala	Ser	Pro	Pro 925	Arg	Pro	His
Asp (SEQ	ID NO:3)										



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#### 17/20

Met His Val Pro Gly Glu Glu Asn Gly Glu Pro Leu Ala Ile Val Gly 10 Met Ala Cys Arg Leu Pro Gly Gly Val Ala Ser Pro Glu Asp Leu Trp Arg Leu Leu Glu Ser Gly Gly Asp Gly Ile Thr Ala Phe Pro Thr Asp 40 Arg Gly Trp Asp Val Asp Gly Leu Tyr Asp Pro Asp Pro Asp His Pro Gly Thr Ser Thr Val Arg His Gly Gly Phe Leu Ala Gly Val Ala Asp Phe Asp Ala Ala Phe Phe Gly Ile Ser Pro Arg Glu Ala Leu Ala Met Asp Pro Gln Gln Arg Leu Val Leu Glu Thr Ser Trp Glu Ala Leu Glu 105 His Ala Gly Ile Leu Pro Glu Ser Leu Arg Gly Ser Asp Thr Gly Val 120 Phe Met Gly Ala Phe Ser Asp Gly Tyr Gly Leu Gly Thr Asp Leu Gly 135 140 Gly Phe Gly Ala Thr Gly Thr Gln Thr Ser Val Leu Ser Gly Arg Leu 155 150 Ser Tyr Phe Tyr Gly Leu Glu Gly Pro Ala Val Thr Val Asp Thr Ala 165 170 Cys Ser Ser Ser Leu Val Ala Leu His Gln Ala Gly Gln Ser Leu Arg 185 Ser Gly Glu Cys Ser Leu Ala Leu Val Gly Gly Val Thr Val Met Ala 200 Ser Pro Ser Gly Phe Val Glu Phe Ser Gln Gln Arg Gly Leu Ala Pro Asp Ala Arg Cys Lys Ala Phe Ala Asp Ala Ala Asp Gly Thr Gly Phe 235 230 Ala Glu Gly Ser Gly Val Leu Ile Val Glu Arg Leu Ser Asp Ala Glu 250 Arg Asn Gly His Arg Val Leu Ala Val Val Arg Gly Ser Ala Val Asn 265 Gln Asp Gly Ala Ser Asn Gly Leu Ser Ala Pro Asn Gly Pro Ser Gln 280 Glu Arg Val Ile Arg Gln Ala Leu Ala Asn Ala Gly Leu Thr Pro Ala 295 300 Asp Val Asp Ala Val Glu Ala His Gly Thr Gly Thr Arg Leu Gly Asp 310 315 Pro Ile Glu Ala Gln Ala Val Leu Ala Thr Tyr Gly Gln Gly Arg Asp 330 Thr Pro Val Leu Leu Gly Ser Leu Lys Ser Asn Ile Gly His Thr Gln 345 Ala Ala Ala Gly Val Ala Gly Val Ile Lys Met Val Leu Ala Met Arg His Gly Thr Leu Pro Arg Thr Leu His Val Asp Thr Pro Ser Ser His 375 380 Val Asp Trp Thr Ala Gly Ala Val Glu Leu Leu Thr Asp Ala Arg Pro 395 Trp Pro Glu Thr Asp Arg Pro Arg Arg Ala Gly Val Ser Ser Phe Gly 410 405 Val Ser Gly Thr Asn Ala His Val Leu Leu Glu Ala His Pro Ala Gly 425 Glu Pro Pro Ala Glu Glu Pro Ser Ala Ser Lys Pro Gly Glu Pro Leu 440 445 435



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Ile	Ala 450	Thr	Pro	Leu	Thr	Pro 455	Leu	Pro	Val	Ser	Ala 460	Arg	Thr	Ala	Thr
		Asp	Gly	Gln	Val 470		Arg	Leu	Arg	Glu 475		Leu	Ala	Ala	Arg 480
465 Pro	Gly	His	Asp			Ala	Ile	Ala			Leu	Leu	Ala		
ml	m)	Dl	D	485	7	71-	17.7	T 011	490	7 an	7 an	Λan	Val	495	
			Pro 500					505					510		
Gly	Thr	Ala 515	Leu	Thr	Glu	Pro	Arg 520	Thr	Val	Phe	Val	Phe 525	Pro	Gly	Gln
Gly	Pro 530	Gln	Trp	Arg	Gly	Met 535	Gly	Val	Glu	Leu	Met 540	Ala	Ala	Ser	Pro
Val		Ala	Ala	Arq	Met	Arq	Gln	Cys	Ala	Asp	Ala	Leu	Ile	Pro	His
545					550	_		-		555					560
	Gly	Trp	Asp	Pro 565	Ile	Ala	Met	Leu	Asp 570	Asp	Pro	Glu	Val	Thr 575	Arg
Arg	Val	Asp	Val 580		His	Pro	Val	Cys 585	-	Ala	Val	Met	Val 590		Leu
ת ד ת	λΙα	1751	Trp	Glu	Δla	Δla	Glv	-	Δra	Pro	Asn	Δla		Tle	Glv
AIG	Ата	595	ırp	Giu	AIG	AIG	600	vul	9	110	пор	605	· u _	110	017
His	Ser		Gly	Glu	Tle	Δla		Ala	Cvs	Va 1	Ala		Ala	Leu	Thr
1115	610	OIII	017	014		615			<b>-</b> 1		620				
T.eu		Asp	Gly	Ala	Ara		Val	Ala	Leu	Ara		Val	Leu	Leu	Leu
625	014		<b>-</b> 1		630					635					640
	Ara	Glu	Leu	Ala		Ara	Glv	Ala	Met		Ser	Val	Ala	Leu	
		0		645	1	5	1		650	1				655	
Ala	Ala	Asp	Val		Ala	Asp	Ala	Ala		Ile	Asp	Gly	Val	Trp	Val
		p	660			F		665	3		- 1	4	670	- 1	
Ala	Gly	Arg 675	Asn	Gly	Ala	Thr	Thr 680	Thr	Thr	Val	Ala	Gly 685	Arg	Pro	Asp
Ala			Thr	Leu	Ile			Tyr	Glu	Ala			Val	Trp	Val
3	690	T1 -	77.	17- 1	7. ~ ~	695	D×o	The	uia	Th.~	700	Dho	v-1	7 an	Dro
	Arg	me	Ala	vai	710	Cys	PIO	1111	птъ	715	PLO	Pile	vai	Asp	720
705	Т	λαν	Glu	Len		λνα	Tla	V=1	Δla		Thr	Thr	Ser	Δra	
	_	_		725					730					735	
			Pro 740					745					750		
Pro	Leu	Asp 755	Asp	Glu	Tyr		Phe 760					His 765		Val	Gly
Phe	Ala 770	Thr	Ala	Val	Thr	Ala 775	Ala	Arg	Glu	Pro	Gly 780	Asp	Thr	Val	Phe
Val 785		Val	Ser	Ala	His 790	Pro	Val	Leu	Leu	Pro 795	Ala	Ile	Asp	Gly	Ala 800
	17-1	77.	Thr	Tou		7 20	Glv	Glv	Glv		Hic	Δra	Len	T.e.11	
				805					810					815	
Ala	Leu	Ala	Glu 820	Ala	His	Thr	Thr	Gly 825	Val	Pro	Val	Asp	Trp 830	Ala	Ala
Val	Val	Pro 835	Ala	Thr	Ala	Thr	Ala 840	His	Asp	Leu	Pro	Thr 845	Tyr	Ala	Phe
His	His		Arg	Tyr	Trp	Ile		His	Trp	Leu	Pro	Ser	Gly	Glu	Ala
	850					855					860				
	Pro	Arg	Pro	Ala		Asp	Thr	Glu	Ser		Thr	Gly	Arg	Thr	
865	0	D	D	N	870 Dxo	111-	7 ~~	/er	O TD	875	4.)				880
Ala	ser	Pro	Pro	Arg 885	Pro	HIS	Asp	(SE	עד ט	NO:	± /				



Met 1	His	Val	Pro	Gly 5	Glu	Glu	Asn	Gly	Glu 10	Pro	Leu	Ala	Ile	Val 15	Gly
Met	Ala	Cys	Arg 20	Leu	Pro	Gly	Gly	Val 25	Ala	Ser	Pro	Glu	Asp 30	Leu	Trp
Arg	Leu	Leu 35	Glu	Ser	Gly	Gly	Asp 40	Gly	Ile	Thr	Ala	Phe 45	Pro	Thr	Asp
Arg	Gly 50	Trp	Asp	Val	Asp	Gly 55	Leu	Tyr	Asp	Pro	Asp 60	Pro	Asp	His	Pro
Gly 65	Thr	Ser	Thr	Val	Arg 70	His	Gly	Gly	Phe	Leu 75	Ala	Gly	Val	Ala	Asp 80
Phe	Asp	Ala	Ala	Phe 85	Phe	Gly	Ile	Ser	Pro 90	Arg	Glu	Ala	Leu	Ala 95	Met
_			100					105					110	Leu	
		115					120					125		Gly	
	130					135					140			Leu	
Gly 145	Phe	Gly	Ala	Thr	Gly 150	Thr	Gln	Thr	Ser	Val 155	Leu	Ser	Gly	Arg	Leu 160
	Tyr	Phe	Tyr	Gly 165		Glu	Gly	Pro	Ala 170	Val	Thr	Val	Asp	Thr 175	Ala
			180					185					190	Leu	
	_	195	_				200					205		Met	
	210					215					220			Ala	
225		-	_		230					235				Gly	240
		_		245					250					Ala 255	
			260					265					270	Val	
	_	275					280					285		Ser	
	290					295					300			Pro	
305		_			310					315				Gly	320
				325					330					Arg 335	
			340					345					350	Thr	
		355					360					365		Met	
	370					375					380			Ser	
Val 385	Asp	Trp	Thr	Ala	Gly 390	Ala	Val	Glu	Leu	Leu 395	Thr	Asp	Ala	Arg	Pro 400
	Pro	Glu	Thr	Asp 405		Pro	Arg	Arg	Ala 410		Val	Ser	Ser	Phe 415	Gly
Val	Ser	Gly	Thr		Ala	His	Val			Glu	Ala	His		Ala	Gly
			420					425					430		
Glu		Pro 435	Ala	Glu	Glu	Pro	Ser 440	Ala		Lys	Pro	Gly 445		Pro	Leu

O di l'Aren Aren

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#### 20/20

Ile Ala Thr Pro Leu Thr Pro Leu Pro Val Ser Ala Arg Thr Ala Thr 455 Ala Leu Asp Gly Gln Val Arg Arg Leu Arg Glu His Leu Ala Ala Arg 475 470 Pro Gly His Asp Pro Arg Ala Ile Ala Ala Gly Leu Leu Ala Arg Arg 485 490 Thr Thr Phe Pro His Arg Ala Val Leu Leu Asp Asp Val Val Thr 505 500 Gly Thr Ala Leu Thr Glu Pro Arg Thr Val Phe Val Phe Pro Gly Gln 520 Gly Pro Gln Trp Arg Gly Met Gly Val Glu Leu Met Ala Ala Ser Pro 535 Val Phe Ala Ala Arg Met Arg Gln Cys Ala Asp Ala Leu Ile Pro His 555 550 Thr Gly Trp Asp Pro Ile Ala Met Leu Asp Asp Pro Glu Val Thr Arg 570 565 Arg Val Asp Val Val His Pro Val Cys Trp Ala Val Met Val Ser Leu 585 Ala Ala Val Trp Glu Ala Ala Gly Val Arg Pro Asp Ala Val Ile Gly 600 His Ser Gln Gly Glu Ile Ala Ala Cys Val Ala Gly Ala Leu Thr 615 Leu Glu Asp Gly Ala Arg Leu Val Ala Leu Arg Ser Val Leu Leu 630 635 Leu Arg Glu Leu Ala Gly Arg Gly Ala Met Gly Ser Val Ala Leu Pro 645 650 Ala Ala Asp Val Glu Ala Asp Ala Ala Arg Ile Asp Gly Val Trp Val 665 Ala Gly Arg Asn Gly Ala Thr Thr Thr Thr Val Ala Gly Arg Pro Asp 680 Ala Val Glu Thr Leu Ile Ala Asp Tyr Glu Ala Arg Gly Val Trp Val 695 Arg Arg Ile Ala Val Asp Cys Pro Thr His Thr Pro Phe Val Asp Pro 715 710 Leu Tyr Asp Glu Leu Gln Arg Ile Val Ala Asp Thr Thr Ser Arg Thr 730 725 Pro Glu Ile Pro Trp Phe Ser Thr Ala Asp Glu Arg Trp Ile Asp Ala 745 740 Pro Leu Asp Asp Glu Tyr Trp Phe Arg Asn Met Arg His Pro Val Gly 760 Phe Ala Thr Ala Val Thr Ala Ala Arg Glu Pro Gly Asp Thr Val Phe 780 775 Val Glu Val Ser Ala His Pro Val Leu Leu Pro Ala Ile Asp Gly Ala 790 795 Thr Val Ala Thr Leu Arg Arg Gly Gly Val His Arg Leu Leu Thr 805 810 Ala Leu Ala Glu Ala His Thr Thr Gly Val Pro Val Asp Trp Ala Ala 825 Val Val Pro Ala Thr Ala Thr Ala His Asp Leu Pro Thr Tyr Ala Phe 840 845 His His Glu Arg Tyr Trp Ile Ser His Trp Leu Pro Ser Gly Glu Ala 855 860 His Pro Arg Pro Ala Asp Asp Thr Glu Ser Gly Thr Gly Arg Thr Glu 870 Ala Ser Pro Pro Arg Pro His Asp (SEQ ID NO:5) 885